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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	8

DATE MAILED: 11/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/895,040	SHANNON ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *16-32,37-44,46-48 and 52-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,33-36,45 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed August 26, 2002. Currently, claims 1-56 are pending. Claims 16-32, 37-44, 46-48, 52-56 have been withdrawn as drawn to non-elected subject matter.

Election/Restrictions

2. Applicant's election without traverse of Group I (Claims 1-15, 33-369, 45, 49-51) in Paper No. 7 is acknowledged.

Claims 16-32, 37-44, 46-48, 52-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

The requirement is still deemed proper and is therefore made FINAL.

Priority

3. This application claims priority to several PCT applications in addition to CIP of 09/864,761, filed May 23, 2001. The priority documents contain no description of SEQ ID NO: 1, 2, 3, 4, 6 or 7. Therefore, the instant claims enjoy the benefit of June 29, 2001, the instant filing date.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

For example on pages 20, 78, websites are included

5. The specification is objected to because the specification contains several _____ for Accession Numbers. For example, page 18, 53, 129, 102 contain no number within the blank provided. Appropriate correction is required. Applicant is reminded the no new matter may be added.

Claim Objections

6. Claim 49 is objected to because Claim 49 relies upon non-elected claims. Claims 46-48 are drawn to non-elected subject matter. Therefore, Claim 49 has been examined to the extend that it reads upon the elected group.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-15, 33-36, 45, 49-51 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claims are drawn to isolated nucleic acids comprising SEQ ID NO: 1 or 2; a degenerate variant of SEQ ID NO: 2; a nucleic acid which encodes SEQ ID NO: 3; a nucleic acid which encodes SEQ ID NO: 2 with conservation changes of amino acids; at least 17 contiguous nucleotides of SEQ ID NO: 4; at least 17 contiguous nucleotides of

SEQ ID NO: 6; degenerate variants of SEQ ID NO: 6; nucleic acid which encode SEQ ID NO: 7.

The specification teaches that SEQ ID NO: 1 is the full length cDNA with untranslated regions. The specification teaches SEQ ID NO: 2 is the open reading frame. The specification teaches SEQ ID NO: 3 is the full amino acid sequence. The human GRBP2 cDNA spans 3484 nucleotides and contains an open reading frame from nucleotide 21 through and including nucleotide 2081. The predicted protein is 686 amino acids with a molecular weight of 77.0 kD. The specification asserts that the reading frame appear full length because it begins with a methionine and terminates with a stop codon (page 129). The specification teaches SEQ ID NO: 4 is the 5' untranslated region and initial coding sequence. SEQ ID NO: 6 is the 5' untranslated region not in the alternative minor form disclosed prior to the instant filing date. SEQ ID NO: 7 is the amino acid sequence not found in the alternative form. The specification teaches that GRBP2 interacts with GTPase Rho. The specification asserts that levels of human GRBP2 mRNA in cells may be assessed to diagnose oncogenesis (page 124). The specification asserts that Tables 1 and 2 show significant expression of exons 2, 3, 6, 11 and 15 in kidney, adrenal, adult liver, bone marrow, brain, fetal liver, heart, hela, lung, placenta, prostate and skeletal muscle (page 128). The specification teaches that the human GRBP2 gene can be mapped to human chromosome 19q12 (page 129). In a BLAST search the GRBP1 mouse shares 46% amino acid identity and 61% amino acid identity over 583 amino acids (page 131). Additionally another mouse gene is 85% identical at the amino acid level and 91% identity over 686 amino acids

(page 131). The specification provides that certain protein domains and overall structural organization are shared with mouse Grbp1 and Grbp2 (page 132). The specification hypothesizes that the "shared structural features strongly imply that human GRBP2 and murine Grbp2 play a role similar to that of mouse Grbp1 as a putative adaptor protein that interacts with both the small GRPase Rho as well as elements of the actin cytoskeleton, with a potential role as a proto-oncogene/oncogene (page 132). The human GRBP2 contains HR1 domain, residues 38-98 of SEQ ID NO: 3 and a PDZ domain at residues 513-594 of SEQ ID NO: 3 (page 132). The specification provides the standard protocol for determining whether an association between increased GRBP2 expression is indicative of neoplasia. The specification provides that certain chromosomal regions may to locations known to be associated with diseases.

In analyzing each of the tests for establishing utility, GRBP2, SEQ ID NO: 1-4, 6-7, fail to have either a specific or substantial or a well-established utility. First the specification asserts that the utility for the GRBP2 nucleic acids are for expression analysis indicative of neoplasia. The art does not support the assertion of the association between GRBP2 and neoplasia.

It is noted that the utility of the invention must have existed at the time of filing. However, the post filing date art (Saatcioglu, WO 01/72962, October 4, 2001) demonstrates that PSL22 gene and mRNA, which is over 99% identical with SEQ ID NO: 1, 2 and 3 of the instant application, is expressed in various human tissues including prostate, kidney, pancreas and colon. Saatcioglu teaches the androgen

regulation of PSL22 was examined in PC3 and DU145 cells, in androgen-independent prostate cancer cell lies and in CWR22R cells. The analysis demonstrates that PSL22 is androgen regulated in LNCaP cells, where it is highly expressed, but not in androgen regulated PC2 and Du145 cell (page 62). This analysis has not demonstrated any overexpression in neoplasia generally, nor in prostate cancer because there does not appear to be any correlation between normal and cancerous cells presented.

Turning to the teachings in the specification, the asserted utility is neither specific nor substantial as a marker for prostate cancer. A substantial utility is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. The asserted utility of a marker for neoplasia requires carrying out further research to reasonably confirm a "real world" use. The specification asserts that "diseases that map to the human GRBP2 chromosomal region" including oncogene liposarcoma, ichthyosis congentita III and benign familial infantile convulsions (page 139). This passage illustrates that as of the time of filing, the specification has not performed any analysis studies to determine whether GRBP2, namely SEQ ID NO: 1-4, 6-7, has altered expression and whether the altered expression is strongly correlated with any particular neoplasia in particular. The specification demonstrated the expression level of GRBP2 in numerous normal tissues including, kidney, adrenal, adult liver, bone marrow, brain, fetal liver, heart, hela, lung, placenta, prostate and skeletal muscle (page 128). Therefore, the skilled artisan would be required to perform further research to confirm the use of SEQ ID NO: 1-4, 6-7 as a marker for neoplasia. There is

no indication in the specification whether the marker is expressed in both normal and disease tissue or whether the over or underexpression of the nucleic acid is indicative of a disease state. Additionally, the specification has provided no threshold or range which would indicate to the skilled artisan how to determine whether a tissue was neoplastic. There is no suggestion in the specification whether the maker is associated with all neoplastic tissue or whether the marker is specific for a specific neoplasia. Therefore, upon determining whether there is expression within a set of neoplsia, the range of expression as indicative of normal, benign or neoplastic tissue, the skilled artisan would be required to interpret these results to obtain a meaningful real world use. Each of these inquiries are required prior to the skilled artisan being able to use the claimed invention.

Additionally, the assertions in the specification which hypothesize that the "shared structural features strongly imply that human GRBP2 and murine Grbp2 play a role similar to that of mouse Grbp1 as a putative adaptor protein that interacts with both the small GRPase Rho as well as elements of the actin cytoskeleton, with a potential role as a proto-oncogene/oncogene (page 132)" do not provide evidence that the nucleic acid is either a proto-oncogene nor an oncogene. The utility of Grbp1 does not appear to be settled in the art. The specification merely asserts that the protein interacts with the small Rpase Rho and elements of the actin cytoskeleton. Neither of these functions of the protein provide a real world use for the protein. The specification nor the art has provided any general teachings of utility for proteins which interact with Rho or with PDZ domain containing proteins.

Moreover, with respect to the specific variations or nucleic acid fragments comprised in larger sequences, the specification fails to provide any guidance as how to use these nucleic acids. Since the nucleic acids which minimally contain 17 nucleic acids are found in various species, in various genes, there is no indication of how to use these nucleic acids as indicative of neoplasia. For example, as provided below in the 102 rejection, Sonstegard teaches a nucleic acid from Bos Taurus which comprsises nucleotides 37-64 of SEQ ID NO: 4. There is no indication of how to use this sequence as predictive of neoplasia.

With respect to the conservative substitutions within SEQ ID NO: 3, the specification fails to teach any conservative substitutions which maintain the function of the protein. Since the specification fails to provide any function for the protein of SEQ ID NO: 3, the conservative substitutions therefore would also lack utility. However, in the event that a utility were established for the specific sequence of SEQ ID NO: 3, there is no teaching which amino acids may be conservatively substituted such that the function of the protein would be maintained. There is no teachings as to the critical regions within the protein, no teachings as how many changes may be made while still maintaining the function or any other guidance as to how the protein may be altered to maintain a structure function relationship.

As noted by Brenner v. Manson, 383 U.S. 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing...a patent is not a hunting license. It is not a reward for the search, but compensation for its successful

conclusion". Therefore, since the specification fails to provide a well established or a specific and substantial utility, the claimed invention lacks utility.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-15, 33-36, 45, 49-51 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The claims are broadly drawn to isolated nucleic acids comprising SEQ ID NO: 1 or 2; a degenerate variant of SEQ ID NO: 2; a nucleic acid which encodes SEQ ID NO: 3; a nucleic acid which encodes SEQ ID NO: 2 with conservation changes of amino acids; at least 17 contiguous nucleotides of SEQ ID NO: 4; at least 17 contiguous nucleotides of SEQ ID NO: 6; degenerate variants of SEQ ID NO: 6; nucleic acid which encode SEQ ID NO: 7.

The specification teaches that SEQ ID NO: 1 is the full length cDNA with untranslated regions. The specification teaches SEQ ID NO: 2 is the open reading frame. The specification teaches SEQ ID NO: 3 is the full amino acid sequence. The human GRBP2 cDNA spans 3484 nucleotides and contains an open reading frame from nucleotide 21 through and including nucleotide 2081. The predicted protein is 686 amino acids with a molecular weight of 77.0 kD. The specification asserts that the

reading frame appear full length because it begins with a methionine and terminates with a stop codon (page 129). The specification teaches SEQ ID NO: 4 is the 5' untranslated region and initial coding sequence. SEQ ID NO: 6 is the 5' untranslated region not in the alternative minor form disclosed prior to the instant filing date. SEQ ID NO: 7 is the amino acid sequence not found in the alternative form. The specification teaches that GRBP2 interacts with GTPase Rho. The specification asserts that levels of human GRBP2 mRNA in cells may be assessed to diagnose oncogenesis (page 124). The specification asserts that Tables 1 and 2 show significant expression of exons 2, 3, 6, 11 and 15 in kidney, adrenal, adult liver, bone marrow, brain, fetal liver, heart, hela, lung, placenta, prostate and skeletal muscle (page 128). The specification teaches that the human GRBP2 gene can be mapped to human chromosome 19q12 (page 129). In a BLAST search the GRBP1 mouse shares 46% amino acid identity and 61% amino acid identity over 583 amino acids (page 131). Additionally another mouse gene is 85% identical at the amino acid level and 91% identity over 686 amino acids (page 131). The specification provides that certain protein domains and overall structural organization are shared with mouse Grbp1 and Grbp2 (page 132). The specification hypothesizes that the "shared structural features strongly imply that human GRBP2 and murine Grbp2 play a role similar to that of mouse Grbp1 as a putative adaptor protein that interacts with both the small GRPase Rho as well as elements of the actin cytoskeleton, with a potential role as a proto-oncogene/oncogene (page 132). The human GRBP2 contains HR1 domain, residues 38-98 of SEQ ID NO: 3 and a PDZ domain at residues 513-594 of SEQ ID NO: 3 (page 132). The

specification provides the standard protocol for determining whether an association between increased GRBP2 expression is indicative of neoplasia. The specification provides that certain chromosomal regions may to locations known to be associated with diseases.

The post filing date art (Saatcioglu, WO 01/72962, October 4, 2001) demonstrates that PSL22 gene and mRNA, which is over 99% identical with SEQ ID NO: 1, 2 and 3 of the instant application, is expressed in various human tissues including prostate, kidney, pancreas and colon. Saatcioglu teaches the androgen regulation of PSL22 was examined in PC3 and DU145 cells, in androgen-independent prostate cancer cell lies and in CWR22R cells. The analysis demonstrates that PSL22 is androgen regulated in LNCaP cells, where it is highly expressed, but not in androgen regulated PC2 and Du145 cell (page 62). This analysis has not demonstrated any overexpression in neoplasia generally, nor in prostate cancer because there does not appear to be any correlation between normal and cancerous cells presented.

Turning to the teachings in the specification, the skilled artisan would be unable to use the claimed nucleic acids as a marker for prostate cancer absent additional undue experimentation. While one could conduct additional experimentation to determine whether, e.g. the nucleic acids of ESQ ID NO: 1-4, 6-7 at certain levels might be associated with, e.g. certain types of neoplasia, the outcome of such research cannot be predicted, and such further research and experimentation are both unpredictable and undue. The specification asserts that "diseases that map to the human GRBP2 chromosomal region" including oncogene liposarcoma, ichthyosis

congentita III and benign familial infantile convulsions (page 139). This passage illustrates that as of the time of filing, the specification has not performed any analysis studies to determine whether GRBP2, namely SEQ ID NO: 1-4, 6-7, has altered expression and whether the altered expression is strongly correlated with any particular neoplasia in particular. The specification demonstrated the expression level of GRBP2 in numerous normal tissues including, kidney, adrenal, adult liver, bone marrow, brain, fetal liver, heart, hela, lung, placenta, prostate and skeletal muscle (page 128). Therefore, the skilled artisan would be required to perform further research to confirm the use of SEQ ID NO: 1-4, 6-7 as a marker for neoplasia. There is no indication in the specification whether the marker is expressed in both normal and disease tissue or whether the over or underexpression of the nucleic acid is indicative of a disease state. Additionally, the specification has provided no threshold or range which would indicate to the skilled artisan how to determine whether a tissue was neoplastic. There is no suggestion in the specification whether the maker is associated with all neoplastic tissue or whether the marker is specific for a specific neoplasia. Therefore, upon determining whether there is expression within a set of neoplsia, the range of expression as indicative of normal, benign or neoplastic tissue, the skilled artisan would be required to interpret these results to obtain a meaningful real world use. Each of these inquiries are required prior to the skilled artisan being able to use the claimed invention.

Additionally, the assertions in the specification which hypothesize that the "shared structural features strongly imply that human GRBP2 and murine Grbp2 play a role similar to that of mouse Grbp1 as a putative adaptor protein that interacts with both

the small GRPase Rho as well as elements of the actin cytoskeleton, with a potential role as a proto-oncogene/oncogene (page 132)" do not provide evidence that the nucleic acid is either a proto-oncogene nor an oncogene. The utility of Grbp1 does not appear to be settled in the art. The specification merely asserts that the protein interacts with the small Rpase Rho and elements of the actin cytoskeleton. Neither of these functions of the protein provide a skilled artisan to make and use for the nucleic acid. The specification nor the art has provided any general teachings of utility for proteins which interact with Rho or with PDZ domain containing proteins.

Moreover, with respect to the specific variations or nucleic acid fragments comprised in larger sequences, the specification fails to provide any guidance as how to use these nucleic acids. Since the nucleic acids which minimally contain 17 nucleic acids are found in various species, in various genes, there is no indication of how to use these nucleic acids as indicative of neoplasia. For example, as provided below in the 102 rejection, Sonstegard teaches a nucleic acid from Bos Taurus which comprsises nucleotides 37-64 of SEQ ID NO: 4. There is no indication of how to use this sequence as predictive of neoplasia.

With respect to the conservative substitutions within SEQ ID NO: 3, the specification fails to teach any conservative substitutions which maintain the function of the protein. Since the specification fails to provide any function for the protein of SEQ ID NO: 3, the conservative substitutions therefore would also lack a use. However, in the event that a use were established for the specific sequence of SEQ ID NO: 3, there is no teaching which amino acids may be conservatively substituted such that the

function of the protein would be maintained. There is no teachings as to the critical regions within the protein, no teachings as how many changes may be made while still maintaining the function or any other guidance as to how the protein may be altered to maintain a structure function relationship.

Additionally, Claims 33-36 recite a pharmaceutical composition comprising the nucleic acid with a pharmaceutically acceptable excipient. The claims are not enabled for a pharmaceutical use. The specification has provided no evidence that the nucleic acid in a pharmaceutically acceptable excipient has any pharmaceutical use. Similarly, Claim 49 which has the intended use for in vivo administration fails to be enabled for the full scope of the claim. The specification has not provided any evidence or studies that the nucleic acid may be used as either a pharmaceutical or in in vivo administration. Since the specification has conducted neither in vitro studies nor in vivo studies with respect to neoplasia association, it is unpredictable that the administration of the nucleic acid would have any affects on neoplasia. Therefore, further undue and unpredictable experimentation would be required.

With respect to the enablement as to how to make a nucleic acid which has a useful activity, the specification has not provided which nucleic acid variants which are claimed have the specific activity asserted. With respect to a nucleic acid which encodes SEQ ID NO: 3 with conservation changes of amino acids, the specification has not described which conservative amino acid changes will result in a functioning polypeptide. Therefore, there is no structure function relationship which has been described as required by the Written guidelines where a partial structure is defined.

The specification has not taught which nucleic acids comprising at least 17 contiguous nucleotides of SEQ ID NO: 4, or at least 17 contiguous nucleotides of SEQ ID NO: 6 has the asserted utility. For example, the claims read upon homo sapiens rhophilin-like protein, a clone from 3p, a clone from chromosome 19, in addition to nucleic acids from chromosome 11, 16, rabbit myosin heavy chain mRNA, halobacterium sp. NRC-1 section 90 of 170, oryza sativa chromosome 8, RRE.Mut (B), HIV rev response element RRE.Mut (A), and wheat (see sequence search results). It is unclear which of these nucleic acids encompassed by the claims have the asserted activity of association with neoplasia. The amino acid sequence of SEQ ID NO: 7 is only 23 amino acids in length. This partial structure appears to be found in several nucleic acids which have not been taught by the instant specification. Therefore making and using these nucleic acids would require further unpredictable and undue experimenation.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-15, 33-369, 45, 49-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to nucleic acids comprising SEQ ID NO: 1 or 2; a degenerate variant of SEQ ID NO: 2; a nucleic acid which encodes SEQ ID NO: 3; a nucleic acid which encodes SEQ ID NO: 2 with conservation changes of amino acids; at least 17 contiguous nucleotides of SEQ ID NO: 4; at least 17 contiguous nucleotides of SEQ ID NO: 6; degenerate variants of SEQ ID NO: 6; nucleic acid which encode SEQ ID NO: 7.

The specification teaches that SEQ ID NO: 1 is the full length cDNA with untranslated regions. The specification teaches SEQ ID NO: 2 is the open reading frame. The specification teaches SEQ ID NO: 3 is the full amino acid sequence. The specification teaches SEQ ID NO: 4 is the 5' untranslated region and initial coding sequence. SEQ ID NO: 6 is the 5' untranslated region not in the alternative minor form disclosed prior to the instant filing date. SEQ ID NO: 7 is the amino acid sequence not found in the alternative form.

With respect to a nucleic acid which encodes SEQ ID NO: 3 with conservation changes of amino acids, the specification has not described which conservative amino acid changes will result in a functioning polypeptide. Therefore, there is no structure function relationship which has been described as required by the Written guidelines where a partial structure is defined.

With respect to a nucleic acid comprising at least 17 contiguous nucleotides of SEQ ID NO: 4, or at least 17 contiguous nucleotides of SEQ ID NO: 6, the specification

has not taught a representative number of nucleic acids which minimally contain 17 nucleotides of SEQ ID NO: 4 or 6. As illustrates below, in the rejections under 102, the claims read upon numerous nucleic acids which have not been described. For example, the claims read upon homo sapiens rhophilin-like protein, a clone from 3p, a clone from chromosome 19, in addition to nucleic acids from chromosome 11, 16, rabbit myosin heavy chain mRNA, halobacterium sp. NRC-1 section 90 of 170, oryza sativa chromosome 8, RRE.Mut (B), HIV rev response element RRE.Mut (A), and wheat (see sequence search results). Thus, the specification has not provided a representative number of species for the large genus of nucleic acids minimally containing 17 contiguous nucleotides from SEQ ID NO: 4 and 6.

With respect to nucleic acid which encode SEQ ID NO: 7, the art teaches numerous nucleic acids which encode SEQ ID NO: 7. As provided in the 102 rejections below, SEQ ID NO: 7 encodes rhophilin-like protein mRNA and nucleic acids from chromosomes 3 and 19. Post filing date art also demonstrates that SEQ ID NO: 7 encodes a prostate specific protein PSL22 (WO 01/72962, October 4, 2001). The amino acid sequence of SEQ ID NO: 7 is only 23 amino acids in length. This partial structure appears to be found in several nucleic acids which have not been described by the instant specification.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-15, 33-369, 45, 49-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-15, 33-369, 45, 49-51 are indefinite because the claim contains two viii subcategories. Therefore, in subcategory ix directed to the complement of any one of I-viii, it is unclear whether the claim is directed to both the viii subcategories, the first viii category or the second viii category. Moreover, the Markush group does not end with an "and" prior to the last element. Appropriate correction is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Burbelo et al. (Genbank Accession Number AF268032, June 2, 2001; submitted May 16, 2000).

Burbelo et al. (herein referred to as Burbelo) teaches a nucleic acid from homo sapiens rhophilin-like protein mRNA which comprises 89 contiguous nucleotides from SEQ ID NO: 4 (limitations of Claim 1vi). Nucleotides 8-96 of the nucleic acid taught by Burbelo is 100% identical with nucleotides 1-89 of SEQ ID NO: 4. Moreover, Burbelo teaches 69 contiguous nucleotides of SEQ ID NO: 6 (limitations of Claim 1vii).

Nucleotides 28-96 of Burbelo are 100% identical with nucleotides 1-69 of SEQ ID NO: 6. Burbelo teaches a nucleic acid which encodes SEQ ID NO: 7, namely nucleotides 28-96 (limitations of Claim 1viii).

12. Claims 1 are rejected under 35 U.S.C. 102(a) as being anticipated by Wu et al. (Genbank Accession Number AC025267, October 2000; submitted March 2000).

Wu et al. (herein referred to as Wu) teaches a homo sapiens chromosome 3p clone which comprises 89 contiguous nucleotides of SEQ ID NO: 4 (limitations of Claim 1vi). Nucleotides 4804-4716 of the nucleic acid taught by Wu is 100% identical with nucleotides 1-89 of SEQ ID NO: 4. Moreover, Wu teaches 69 contiguous nucleotides of SEQ ID NO: 6 (limitations of Claim 1vii). Nucleotides 4784-4716 of Wu are 100% identical with nucleotides 1-69 of SEQ ID NO: 6. Wu teaches a nucleic acid which encodes SEQ ID NO: 7, namely nucleotides 4784-4716 (limitations of Claim 1viii).

13. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by DOE Joint Genome Institute (Genbank Accession Number AC008521, April 2000).

DOE Joint Genome Institute teaches a nucleic acid from homo sapiens chromosome 19 clone which comprises 89 contiguous nucleotides from SEQ ID NO: 4 (limitations of Claim 1vi). Nucleotides 48145-48057 of the nucleic acid taught by DOE Joint Genome Institute is 100% identical with nucleotides 1-89 of SEQ ID NO: 4. Moreover, DOE Joint Genome Institute teaches 69 contiguous nucleotides of SEQ ID NO: 6 (limitations of Claim 1vii). Nucleotides 48125-48057 of DOE Joint Genome

Institute are 100% identical with nucleotides 1-69 of SEQ ID NO: 6. DOE Joint Genome Institute teaches a nucleic acid which encodes SEQ ID NO: 7, namely nucleotides 48125-48057 (limitations of Claim 1viii).

14. Claims 1, 4-6, 8-11, 33-36, are rejected under 35 U.S.C. 102(a) as being anticipated by Sonstegard et al (Genbank Accession Number BE478809, August 2000).

With respect to Claims 33-36 directed to a pharmaceutical composition comprising nucleic acids of Claims 1-6 and a pharmaceutically acceptable excipient, because the pharmaceutical language recited in the claims does not impart any particular or new feature, this is interpreted as an "intended use." The composition has not other components other than the components of the nucleic acid and a pharmaceutically acceptable carrier. Vectors are routinely stored in buffers that would be pharmaceutically acceptable.

Sonstegard et al. (herein referred to as Sonstegard) teaches a nucleic acid from Bos Taurus. The nucleic acid sequence comprises 28 contiguous nucleotides of SEQ ID NO: 4. Nucleotides 37-64 of SEQ ID NO: 4 are 100% identical with nucleotides 14-51 of Sonstegard (limitations of Claim 1vi). Sonstegard also teaches that the nucleic acid is in a vector, namely pCMV SPORT6 and in a host cell, namely DH10B (limitations of Claims 4-6, 8-11).

15. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Babij et al. (PNAS, Vol. 88, page 10676-10680, December 1991; Genbank Accession Number M77812).

Babij et al. (herein referred to as Babij) teaches a rabbit myosin heavy chain mRNA nucleic acid which comprises at least 17 nucleotides of SE QID NO: 6, namely 18 nucleotides. The nucleic acid of Babij contains nucleotides 35-52 of SEQ ID NO: 6 at position 3779-3796. Therefore Babij teaches every limitation of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 4-6, 8-15, 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Babij et al. (PNAS, Vol. 88, page 10676-10680, December 1991; Genbank Accession Number M77812)) in view of Sambrook (Molecular Cloning, Expression of Cloned Genes in E. coli, 1992).

With respect to Claims 33-36 directed to a pharmaceutical composition comprising nucleic acids of Claims 1-6 and a pharmaceutically acceptable excipient, because the pharmaceutical language recited in the claims does not impart any particular or new feature, this is interpreted as an "intended use." The composition has not other components other than the components of the nucleic acid and a pharmaceutically acceptable carrier. Vectors are routinely stored in buffers that would be pharmaceutically acceptable.

Babij et al. (herein referred to as Babij) teaches a rabbit myosin heavy chain mRNA nucleic acid which comprises at least 17 nucleotides of SE QID NO: 6, namely 18 nucleotides. The nucleic acid of Babij contains nucleotides 35-52 of SEQ ID NO: 6 at position 3779-3796. Therefore Babij teaches every limitation of the claimed invention.

While Babij teaches an mRNA sequence and a protein translation of the sequences Babij does not specifically teach placing the nucleic acid in a vector and host cell.

However, Sambrook teaches that methods for expressing large amount of protein from a cloned gene include introduction into E. coli. Sambrook teaches that the

expression has proven invaluable in the purification, localization and functional analysis of proteins.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have inserted the nucleic acid of Babij which encodes a protein, into a vector and host cell for expression. The production of the large amounts of protein, as provided by Sambrook allows further analysis including functional analysis. Therefore, producing protein for functional studies would have been obvious at the time the invention was made.

18. Claims 7, 45, 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burbelo et al. (Genbank Accession Number AF268032, June 2, 2001; submitted May 16, 2000) or Wu et al. (Genbank Accession Number AC025267, October 2000; submitted March 2000) or DOE Joint Genome Institute (Genbank Accession Number AC008521, April 2000) or Sonstegard et al (Genbank Accession Number BE478809, August 2000) or Babij et al. (PNAS, Vol. 88, page 10676-10680, December 1991; Genbank Accession Number M77812) in view of DeRisi et al. (Nature Genetics, Vol. 14, pages 457-459, December 1996).

Burbelo et al. (herein referred to as Burbelo) teaches a nucleic acid from homo sapiens rhophilin-like protein mRNA which comprises 89 contiguous nucleotides from SEQ ID NO: 4 (limitations of Claim 1vi). Nucleotides 8-96 of the nucleic acid taught by Burbelo is 100% identical with nucleotides 1-89 of SEQ ID NO: 4. Moreover, Burbelo teaches 69 contiguous nucleotides of SEQ ID NO: 6 (limitations of Claim 1vii).

Nucleotides 28-96 of Burbelo are 100% identical with nucleotides 1-69 of SEQ ID NO: 6. Burbelo teaches a nucleic acid which encodes SEQ ID NO: 7, namely nucleotides 28-96 (limitations of Claim 1viii).

Wu et al. (herein referred to as Wu) teaches a homo sapiens chromosome 3p clone which comprises 89 contiguous nucleotides of SEQ ID NO: 4 (limitations of Claim 1vi). Nucleotides 4804-4716 of the nucleic acid taught by Wu is 100% identical with nucleotides 1-89 of SEQ ID NO: 4. Moreover, Wu teaches 69 contiguous nucleotides of SEQ ID NO: 6 (limitations of Claim 1vii). Nucleotides 4784-4716 of Wu are 100% identical with nucleotides 1-69 of SEQ ID NO: 6. Wu teaches a nucleic acid which encodes SEQ ID NO: 7, namely nucleotides 4784-4716 (limitations of Claim 1viii).

DOE Joint Genome Institute teaches a nucleic acid from homo sapiens chromosome 19 clone which comprises 89 contiguous nucleotides from SEQ ID NO: 4 (limitations of Claim 1vi). Nucleotides 48145-48057 of the nucleic acid taught by DOE Joint Genome Institute is 100% identical with nucleotides 1-89 of SEQ ID NO: 4. Moreover, DOE Joint Genome Institute teaches 69 contiguous nucleotides of SEQ ID NO: 6 (limitations of Claim 1vii). Nucleotides 48125-48057 of DOE Joint Genome Institute are 100% identical with nucleotides 1-69 of SEQ ID NO: 6. DOE Joint Genome Institute teaches a nucleic acid which encodes SEQ ID NO: 7, namely nucleotides 48125-48057 (limitations of Claim 1viii).

Sonstegard et al. (herein referred to as Sonstegard) teaches a nucleic acid from Bos Taurus. The nucleic acid sequence comprises 28 contiguous nucleotides of SEQ ID NO: 4. Nucleotides 37-64 of SEQ ID NO: 4 are 100% identical with nucleotides 14-

51 of Sonstegard (limitations of Claim 1vi). Sonstegard also teaches that the nucleic acid is in a vector, namely pCMV SPORT6 and in a host cell, namely DH10B (limitations of Claims 4-6, 8-11).

Babij et al. (herein referred to as Babij) teaches a rabbit myosin heavy chain mRNA nucleic acid which comprises at least 17 nucleotides of SE QID NO: 6, namely 18 nucleotides. The nucleic acid of Babij contains nucleotides 35-52 of SEQ ID NO: 6 at position 3779-3796. Therefore Babij teaches every limitation of the claimed invention.

Neither Burbelo nor Wu nor DOE Joint Genome Institute nor Sonstegard nor Babij specifically teach attaching the nucleic acid to a solid support or labeling the nucleic acid.

However, DeRisi teaches the use of cDNA microarrays to analyze gene expression patterns, in cancer, for example. The teachings of DeRisi provide that microarrays provide powerful tools for studying complex phenomena. Microarrays may be used to assess expression of genes or cDNA which provides useful insights into human biology and a deeper understanding of the gene pathways involved in pathogenesis. DeRisi also teaches labeling nucleic acids prior to their detection on a solid support for the easy of detection.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the nucleic acids of either Burbelo or Wu or DOE Joint Genome Institute or Sonstegard or Babij to place the nucleic acids on a solid support microarray for the express benefits taught by DeRisi. DeRisi also teaches that nucleic acids may

be labeled for ease of detection. Therefore, the ordinary artisan would have been motivated to placed the nucleic acids taught in the art onto a microarry for the ease of detection using a powerful tool.

Conclusion

19. No claims allowable.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
November 2, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600